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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/713,889	11/14/2003	Benjamin Levinson	WELLSP 3.0-003	1106
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MORRISON & FOERSTER LLP 755 PAGE MILL RD PALO ALTO, CA 94304-1018			EXAMINER KRISHNAN, GANAPATHY	
			ART UNIT	PAPER NUMBER
			1623	
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			12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/713,889	Applicant(s) LEVINSON ET AL.	
	Examiner Ganapathy Krishnan	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 October 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-5, 8-31 and 34-37 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-5, 8-31 and 34-37 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

A Request for Continued Examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed 10/31/2007 has been entered.

The Request for Continued Examination filed 10/31/2007 has been carefully considered. The following information provided in the amendment affects the instant application:

1. Claims 1, 6-7 and 32-33 have been canceled.
2. Remarks drawn to rejections under 35 USC 103(a) of record.

Claims 2-5, 8-31 and 34-37 are pending in the case.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21, 23-28 and 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 21 recites at line 5, subjecting the tin mesoporphyrin formate to a chemical metal insertion process with a metal halide and further recites, to obtain a tin mesoporphyrin halide.

The tin mesoporphyrin formate is subject to a metal insertion and still produces tin mesoporphyrin halide? It is not clear what applicants intend.

According to the method of claim 23, the starting material is hemin. The claim recites that it is reacted with hydrogen and a catalyst to obtain a metal mesoporphyrin formate. Is the iron in the hemin replaced by another metal in this step? Also, where does the formate come from? There is no recitation of a step wherein the hemin is reacted with formic acid. The formate is further subjected to a metal insertion process to obtain a metal mesoporphyrin halide. Is this a new metal that is replacing the metal in the previous step? It is not clear what applicants intend.

Claims that depend from a rejected base claim that is unclear/indefinite are also rendered unclear/indefinite and are rejected for the same reasons.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 29 is rejected under 35 U.S.C. 102(b) as being anticipated by Goel et al (WO 97/05152; document cited in IDS of 10/3/2006).

Goel et al teach a pharmaceutical composition comprising a complex of a cobalt mesoporphyrin (a metal mesoporphyrin) complexed to an amino acid (page 37 line 1 through page 39 line 10; page 49, lines 6-28). This is seen to meet the limitations of instant claim 29.

Claim 29 is a product by process claim, which is a product claim.

Product-by-Process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps.

“Even though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.” In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 2-5, 8-10, 22, 29-31 and 34-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson (US Patent Pub. No. 2003/0100752) in combination with Drummond (Annals of New York Academy of Sciences, 1987, 514, 87-95) and Bettelheim et al (General, Organic and Biochemistry, 1998, page 596), all of record.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Robinson teaches tin mesoporphyrin complexed with amino acid (page 45, claim 1), wherein the substitutions R1-R12 can be H, alkyl or alkenyl and could also be substituents that carry amino acid residues (page 46, left column, middle; page 34, left column, paragraph 200). One of the preferred metal ions complexed to the core is Tin (page 32, paragraph 183). Formulations comprising the porphyrins of Robinson's invention can be optimized to contain between 0.1 and 50 mg (page 33, paragraph 193). The compounds of Robinson can be applied as aqueous solutions (page 35, paragraph 211). This means that the tin-mesoporphyrins of Robinson's invention are water-soluble.

Robinson teaches a method of treating psoriasis using the water-soluble mesoporphyrin compounds complexed with amino acid (page 35, paragraph 211).

Drummond, drawn to metalloporphyrins, teaches control of heme metabolism using tin-protoporphyrins (page 87, introduction, last paragraph). Tin protoporphyrin was by far the most

potent (page 88, Results and Discussion; page 89). Tin protoporphyrin is structurally similar to tin-mesoporphyrin except that the protoporphyrin has an ethylene side chain. In the mesoporphyrin, the ethylene side chain is saturated. According to Robinson (above), the side chain can be an alkenyl. When it is alkenyl, the structure is similar to the protoporphyrin as taught by Drummond.

According to Drummond, tin-protoporphyrins have proved to be innocuous in toxicology studies in animals. Long-term treatment of rats with tin-protoporphyrins resulted in decrease in bilirubin levels (page 90, middle paragraph; page 92, first full paragraph).

Bettelheim in general teaches that amino acids exist as zwitterions and are polar. This renders them water soluble. From this and the teaching of Robinson, one of ordinary skill in the art will recognize that complexing the tin-mesoporphyrins of Robinson with amino acids will enhance the solubility of the mesoporphyrins. Robinson also teaches the use of aqueous solutions of the porphyrins for administration.

Based on the teachings of the prior art above, it would have been obvious to one of ordinary skill in the art at the time the invention was made to make tin mesoporphyrins comprising amino acid residues complexed to the porphyrins, their compositions and use them in a method for treating heme metabolism disorders, hyperbilirubenemia and psoriasis, with a reasonable amount of success since structurally close analogs and their use for the same method of treatment is seen to be taught in the prior art.

One of ordinary skill in the art would be motivated to make tin mesoporphyrins and use them in a method of treatment as instantly claimed because the structurally analogous tin

protoporphyrins, as taught by Drummond, are not toxic and complexing amino acids to the porphyrins would enhance their aqueous solubility.

Even though Drummond teaches protoporphyrins, Robinson's teaching embraces both proto and mesoporphyrins. Proto- and mesoporphyrins are known in the art and are recognized as interchangeable because of their structural similarity. Hence one of ^s ordinary skill in the art would reasonably expect mesoporphyrins as instantly claimed to have the same or substantially similar beneficial therapeutic effects. One of skill in the art would also extend the teachings of the prior art to making tin mesoporphyrins in order to look for more active compounds.

Claims 11-28 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Niedballa et al (US 5,275,801).

Niedballa et al teach a general method of making a water-soluble porphyrin complex (col. 13, line 34 through col. 14, line 12) wherein a porphyrin core structure of formula (I') (col. 7), comprising amino acid residues is obtained by mixing the core structure (I') with amino acid; complexing with metal ions, which includes tin (col. 13, lines 32-43). Secondary reactions like hydrogenation, esterification, and alkylations are all performed according to literature processes known to one of skill in the art (col. 11, lines 3-7). The use of basic solutions like sodium hydroxide in the steps where amino acids are used in a specific form is taught by Niedballa (col. 14, lines 32-39) as well as the use of metal dichlorides for the introduction of the desired metal (col. 13, line 62). The general method of Niedballa results in a solid or pharmaceutically acceptable liquid. Vacuum drying is used to dry the product (col. 14, lines 16-17).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make mesoporphyrins as instantly claimed by making insignificant changes to the method taught in the prior art. One of ordinary skill in the art would be motivated to do so since the method of Niedballa is a general method applicable to the porphyrin core and gives high yields.

Response to Applicants Arguments

Applicants have traversed the rejection arguing that:

1. Drummond describes protoporphyrins and never mentions mesoporphyrins or amino acids. It is unclear how the prior art can be combined to arrive at mesoporphyrins as instantly claimed especially when Robinson describes over 10^{107} compounds.

2. Robinson teaches porphyrin complexes which include sixteen choices, fifteen metals and metal-free porphyrin and does not indicate which of the over 10^{107} agents should be used.

3. The Niedballa reference does not disclose a method for making mesoporphyrins.

Applicants' arguments are not found to be persuasive.

In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992).

Even though Drummond teaches protoporphyrins, Robinson's teaching embraces both proto and mesoporphyrins. Proto- and mesoporphyrins are known in the art and are recognized as interchangeable because of their structural similarity. The compounds of Robinson and Drummond have very closely related structural core. Even though Robinson's structure reads on several compounds, one of skill in the art will prefer to use tin as the central metal in the porphyrin since analogous tin porphyrins as taught by Drummond are potent in the control of heme metabolism and also the presence of tin proved innocuous in toxicology tests. Hence there is a reason to pick tin from among the metals suggested by Robinson. One of the substituents in Robinson's porphyrins is amino acids. Since Bettelheim teaches that amino acids are polar and this makes them water soluble it is logical to choose amino acids as substituents from among the substituents taught by Robinson in order to increase the solubility of the porphyrins by substituting them with amino acids. Hence, based on the suggestion in the prior art it can be seen that there is a teaching as to the preference of amino acids as substitutions and tin as the metal atom in the porphyrin core from among the large genus of Robinson.

Niedballa need not necessarily teach a method for making mesoporphyrin. Niedballa teaches the porphyrin core and according to him all other secondary reactions can be performed by one of skill in the art using standard literature procedures. His teaching is also general and one of skill in the art will be able to recognize this and apply it to the method of making mesoporphyrin as instantly claimed.

Conclusion

Claims 2-5, 8-31 and 34-37 are rejected

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Art Unit: 1623

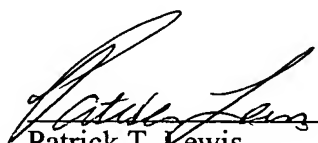
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

GK


Patrick T. Lewis
Primary Patent Examiner
Art Unit 1623